UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,865	10/06/2003	Usha Kasid	GTU-06-1158WO-US	8115

35811 7590 09/25/2006

IP GROUP OF DLA PIPER RUDNICK GRAY CARY US LLP
1650 MARKET ST
SUITE 4900
PHILADELPHIA, PA 19103

EXAMINER	
AEDER, SEAN E	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 10/679,865	**Applicant(s)** KASID ET AL.
	Examiner Sean E. Aeder, Ph.D.	**Art Unit** 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,8 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 7, 8, 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Request for Continued Examination

The request filed on 8/18/06 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 10/679,865 is acceptable and a RCE has been established. An action on the RCE follows.

Claims 1, 7, 8, 10, 36, 38, 42, and 44 were pending.

Claims 36, 38, and 42 have been cancelled by Applicant.

Claim 44 has been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 1, 7, 8, and 10 are currently under consideration.

The text of those sections of Title 35 U.S.C. code not included in this Office Action can be found in a prior Office Action.

Response to Arguments

35 USC § 112, first paragraph, Enablement Rejection

Claims 1, 7, 8, and 10 remain rejected under 35 U.S.C., first paragraph, for failing to comply with the enablement requirement for the reasons of record and the reasons set-forth below.

The claims are broadly drawn to BRCC2 nucleic acids encoding SEQ ID NO:2, vectors comprising said nucleic acids, and host cells comprising said vectors.

The Advisory Action mailed 8/1/06 contains the following text:

"Applicant is not enabled to use the claimed polynucleotides in *any* substantial manner. Applicant relies on data demonstrating that inhibiting raf expression resulted in a decrease in expression of the claimed polynucleotides. Applicant then cites Riedel et al. and states that "such techniques have been used to identify IL-2 as a molecule involved in the raf pathway". Then, upon citing *In re Brana*, indicates that because the claimed polynucleotides were identified by a similar technique used to identify IL-2 as a molecule involved in a raf pathway, Applicant indicates that the claimed polynucleotides can be used in manners similar to those that use IL-2 or that the claimed polynucleotides are involved in a raf pathway related to cancer. However, the teaching of Riedel et al do not identify IL-2 as a member of the raf signaling pathway in a manner similar to the way Applicant identified an association between raf expression and BRCC2 expression. Riedel et al do not inhibit the expression of one polypeptide and conclude that inhibition of a second polypeptide demonstrates that both polypeptides are involved in a similar signaling pathway. Rather, Riedel et al clearly teaches that inhibition of raf expression inhibits IL-2 mediated proliferation (Figure 1, in particular). Combined with previous studies teaching IL-2 mediates raf phosphorylation (page 3146, in particular), the teachings of Riedel et al clearly indicate that raf lies downstream of IL-2 in a pathway regulating cell proliferation. These teachings of Riedel et al do not support that the claimed polynucleotides are involved in an IL-2 mediated proliferation pathway or that the claimed polynucleotides can be used in any substantial manner. Further, one of skill in the art would not conclude that the claimed polynucleotides share any functional or structural characteristics with IL-2. Thus, the claimed polynucleotides and polynucleotides of IL-2 are not "similar known compounds". Further, Examiner is not suggesting that the claimed polynucleotides are not involved in *any* raf pathway;

however, Examiner is stating that the claimed polynucleotides cannot be used in any substantial manner with an expectation of success. Further, there is substantial reasoning to doubt the truth of a statement to the contrary. One of skill in the art would recognized that a concomitant decrease in expression of a novel polynucleotide, such as BRCC2, upon decreasing the expression of a polynucleotide which is enabled to be used in a substantial manner, such as raf, does not indicate that one is enabled to use both polynucleotides in a substantial manner. For instance, the teachings of Patel et al (Molecular Medicine, 1997, 3(10):674-685) clearly demonstrate that inhibition of Raf expression leads to the an increase in KAS-110 and KAS-111 gene expression (page 679, in particular). Further, Patel et al teaches that KAS-110 and KAS-111 are housekeeping genes that are expressed in most normal tissues and several cancer cell tissues (Figure 5 in particular). Thus, Patel et al concludes that Raf modulates the expression of genes with housekeeping functions (page 674, in particular). Therefore, there is no reason to believe that the claimed polynucleotides are not housekeeping genes. One of skill in the art would recognize that housekeeping genes do not have substantial utility. To obviate this rejection, it is suggested that Applicant demonstrate that the claimed polynucleotides would function in a method with substantial utility that was proposed upon filing of the application."

In the RCE filed 8/18/06, Applicant disagrees with the assessment of claims 1, 7, 8, and 10 based on the language utilized in the rejection. Applicant states that the rejection is more in line with 35 U.S.C. 101, and has been mischaracterized as a rejection under 112, first paragraph. Applicant argues that terms such as "substantial utility", "credible utility", and "specific utility" are indicative of a rejection under 101. Applicant further argues that a presumption of utility creates a presumption of utility that is sufficient to satisfy the utility requirement of 101. Applicant further states that the following conclusionary statement is not the appropriate basis upon which to base the rejection: "...[the] Examiner is not suggesting that the claimed polynucleotides are not involved in any raf pathway; however, Examiner is stating that the claimed polynucleotides cannot be used in any substantial manner with an expectation of success" (see advisory action mailed 5/24/06). Applicant further argues that there is a credible and substantial utility for the invention and that there is a reasonable correlation between the polynucleotide activity indicated by Applicants and the proffered therapeutic use. Based on the result that an antisense raf-1 construct increased apoptosis and concomitantly decreased expression of BRCC2 mRNA, Applicant argues that BRCC-2 modulates apoptosis and thereby has a therapeutic/pharmacological utility. Applicant further cites MPEP 2707.01 and states: courts have repeatedly found that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides and immediate benefit to the public and thus satisfies the utility requirement and courts have found utility for therapeutic inventions despite the fact that an applicant is at the very early stages of development in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition. Applicant argues that the result that an antisense raf-1 construct increased apoptosis and concomitantly decreased expression of BRCC2 mRNA establishes a reasonable correlation between

BRCC-2's activity and its therapeutic effect. Applicant further argues that a correlation between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty does not have to be proven. Applicant further argue, and Examiner acknowledges, that actual evidence of success in treating humans where such a utility is asserted does not have to be provided. Applicant further argues that the disclosure is enabling to make and use the claimed invention. Applicant points to the specification to show how to make the invention. Further, Applicant states that the BRCC-2 gene and/or its complement sequences can serve as a probe that forms a hybrid structure with a particular target sequence as well as identify compounds that promote apoptosis of cancer cells, particularly with respect to breast and lung cancer.

The arguments found in the RCE filed 8/18/06 have been carefully considered but are not deemed persuasive. In response to the arguments focused on whether the claimed invention has utility and the assertion that this rejection is more in line with 35 U.S.C. 101 and has been mischaracterized as a rejection under 112, first paragraph, a 35 U.S.C. 101 rejection can be found below addressing said arguments. Further, for the reasons found in the Advisory Action of 5/24/06 and the Office Action of 2/16/06, the result that an antisense raf-1 construct increased apoptosis and concomitantly decreased expression of BRCC2 mRNA does not indicate, or reasonably indicate, any activity of BRCC2. Thus, the specification does not disclose a single activity of BRCC2 mRNA to correlate with any kind of therapeutic use. Although the disclosure is clearly enabling to make the invention, the disclosure is not enabling to use the invention in any substantial manner with an expectation of success.

New Rejection Addressing Arguments Found in RCE

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 7, 8, and 10 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The claims are broadly drawn to BRCC2 nucleic acids encoding SEQ ID NO:2, vectors comprising said nucleic acids, and host cells comprising said vectors.

The specification discloses an antisense raf-1 construct increased apoptosis and concomitantly decreased expression of BRCC2 mRNA (Figure 5).

Based on the assumption that BRCC2 is involved in an apoptotic pathway, the specification prophetically asserts a specific utility for BRCC2 nucleic acids encoding SEQ ID NO:2, vectors comprising said nucleic acids, and host cells comprising said vectors in therapeutic methods as well as methods for identifying compounds that promote apoptosis of cancer cells (paragraphs 33 and 99-101, in particular). It is noted that probing target sequences which have no specific and substantial asserted utility is not a substantial utility.

Following the requirements of the Utility Guidelines, (<http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf>), "substantial utility" is a utility that defines "real world use", wherein utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. In the instant case, the asserted "real world" utility of the claimed invention, based on the assertion that BRCC2 modulates apoptosis, is use of the claimed polynucleotides in therapeutic methods and use of the claimed polynucleotides to identify compounds that promote apoptosis of cancer cells. This asserted "real world" utility is not supported by the specification or the prior art. The prior art provides no example of using the claimed polynucleotides in therapeutic methods and no example of using the claimed polynucleotides to identify compounds that promote apoptosis of cancer cells. Further, the specification neither identifies the functions of the proteins the polynucleotides encode nor does the specification demonstrate that the claimed polynucleotides are associated with any diseases.

One of skill in the art would recognize that if molecules such as the claimed polynucleotides are to be used to detect compounds that promote apoptosis, said claimed polynucleotides must be involved in an apoptotic pathway. As stated in the Advisory Action mailed 8/1/06 and the Office Action mailed 2/16/06, BRCC2 has not been shown to be involved in an apoptotic pathway. The result that an antisense raf-1 construct increased apoptosis and concomitantly decreased expression of BRCC2 mRNA does not indicate, or reasonably indicate, that BRCC2 is involved in apoptosis. Further, one of skill in the art would recognize that apoptotic cell signaling is extremely complex and it would require undue experimentation to determine whether BRCC2 is actually involved in apoptosis.

Further, one of skill in the art would recognized that a concomitant decrease in expression of a novel polynucleotide, such as BRCC2, upon decreasing the expression of a polynucleotide which has substantial utility, such as raf, does not indicate that both polynucleotides have substantial utility. Further, the teachings of Patel et al (Molecular Medicine, 1997, 3(10):674-685) clearly demonstrate that inhibition of Raf expression leads to the an increase in KAS-110 and KAS-111 gene expression (page 679, in particular). Further, Patel et al teaches that KAS-110 and KAS-111 are housekeeping genes that are expressed in most normal tissues and several cancer cell tissues (Figure 5 in particular). Thus, Patel et al concludes that Raf modulates the expression of genes with housekeeping functions (page 674, in particular).. Therefore, there is no reason to believe that the claimed polynucleotides are not housekeeping genes. One of skill in the art would recognize that housekeeping genes would not predictably function as therapeutics and would not be used with any predictability of success in methods of identifying compounds that promote apoptosis.

In regards to using the claimed products in therapeutic methods, therapies, in general, are unpredictable, as underscored by Gura (Science, 1997, 278:1041-1042.) who discusses the potential shortcoming of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with cologenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041 first column, in particular) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive.

Further, those of ordinary skill in the art recognize that treatment in vivo is not predictive. The instant situation is analogous to that of *In re* Brana (34 U.S.P.Q. 2d 1436, 1440 (Fed. Cir. 1995)). A review of *In re Brana* reveals an application that claimed a chemical compound for treating a cancer, wherein the chemical compound was structurally similar to known compounds that have known in vivo use to treat tumors, and more importantly, Applicant provided in vivo data that the claimed compound could treat tumors in mice, hence it was ruled that the claimed compound was enabled for treating tumors. In the instant application, the claims are not drawn to products which have known in vivo ability to give rise to a therapeutic effect. Further, the instant specification provides no in vivo data, particularly demonstrating that the claimed products would predictably give rise to a therapeutic effect in vivo. In view of *In re Brana*, Examiner asserts that successful use of in vivo mouse models of a specific disorder enables compositions for specific therapeutic effects in humans and does not require human clinical testing; however, the instant application is claiming a product which has an asserted therapeutic effect without providing any in vivo data, hence the claimed invention is not enabled for any substantial utility. All of this underscores the criticality of providing workable examples which are not disclosed in the specification, particularly in an unpredictable art, such as therapeutic treatment.

Utility must be in readily available form. One of skill in the art would recognize that novel biological molecules, such as the claimed polynucleotides, lack an established utility and must undergo extensive experimentation to determine an appropriate specific, substantial, and credible utility. It is possible that, after further characterization, the claimed polynucleotides or the proteins in which they encode, might be found to have patentable utility. This further characterization, however, is part of the act of the invention, and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility.

The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where *specific* benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to products with undetermined function or biological significance. Until a specific real world utility is attributed to the claimed products, the claimed invention is incomplete. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polynucleotides and fragments thereof. Because the claimed invention is not supported by a specific and substantial utility for the reasons set forth, credibility of any utility cannot be assessed.

Summary

No claim is allowed. Claims 1, 7, 8, and 10 are rejected under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph, but free of the prior art teaching BRCC2 nucleic acids encoding SEQ ID NO:2, vectors comprising said nucleic acids, and host cells comprising said vectors. The closest prior art for claims 1, 7, 8, and 10 is Birren et al (Homo sapiens chromosome 11 cones RP11-85D24 map 11, 4/22/00), which teaches a sequence >99% identical to SEQ ID NO:2; however, this reference does not teach or suggest BRCC2 nucleic acids encoding SEQ ID NO:2, vectors comprising said nucleic acids, or host cells comprising said vectors.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER